i.e. ARAMIS and CEPAC, for cost-effectiveness analysis in Russia is not possible due to differences in the disease classifications and lack of statistical data. The purpose of this work was the modeling of HIV progression in Russian HIV-infected population. **METHODS:** We develop the Markov model based on transitions through four mutually exclusive health states defined by CD4+ cell count ranges (>500, 351–500, 201–350, and <200 cells/ml) and death and baseline characteristics of high prognostic value, such as viral load, age, sex, and antiretroviral treatment receiving. To identify the model's parameters we used state statistics and publications of the Russian Federal Research Centre for Prevention and Control of AIDS. In order to validate model we calculated life expectancy after diagnosis using Monte-Carlo simulation of treated and non-treated cohorts. To study the influence of treatment on life expectancy we used the 1st line regimen abacavir + zidovudine + lamivudine + enfuvirtide. **RESULTS:** Life expectancy of treated patients is significantly higher compared to patients who did not receive treatment (medians and quartiles 24.6 [22.6; 26.5] and 13.8 years [12.7; 14.4] years, respectively, P<0,001, Mann-Whitney U-test). These results acceptably correspond to the results of cohort studies and clinical trials. Life expectancy is significantly lower for men than for women both with and without treatment. **CONCLUSIONS:** The results of modeling conform the real data from the Russian population. The model is currently being finalized to calculate QALY, ICER, and others.

PRM109

VERIFICATION AND VALIDATION OF HEALTH ECONOMIC MODELS FOR DIABETES

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OBJECTIVES: Published ISPOR guidelines indicate that new economic models should be subjected to through internal testing and debugging. Moreover, evidence that this has been done should be provided. Currently there are few published examples of such internal validation work. The aim of the present analysis was to perform verification and validation analyses of a novel model for Type 1 Diabetes (the PRIME Diabetes Model). **METHODS:** Source code (Java) for the T1D PRIME Diabetes Model was delivered to an independent third party. Program code was reviewed for syntax errors and tested via a separate software environment. This process included using null and extreme input values to test whether the expected outputs were produced. Replication tests using equivalent endpoint values were also performed. Verification queries were resolved by discussion and the findings of the analysis were described in a report. **RESULTS:** Internal validation confirmed all numbers and formulas collected from the literature and examined whether they were correctly implemented in the source code. Face validity was established with regard to the model's structure, use of available clinical evidence, problem formulation and results. Given that the PRIME Diabetes Model is programmed in Java, MATLAB was used to validate model components independently and results were tested at patient mean levels as well as the corner cases of minimum and maximum values in order to ensure the model produced valid results over the entire range of patient characteristics. The model passed both internal and face and validity reviews. **CONCLUSIONS:** Published verification analyses in line with ISPOR guidance for all new health economic models would improve transparency and provide a valuable resource for health care decision makers. Using the PRIME Diabetes Model, the present analysis provides a real-world example of how verification and validation analyses can be performed and reported.

PRM110

IMPACT OF POVERTY ON MULTIDIMENSIONAL INFANT MORTALITY RATE IN BRAZIL

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OBJECTIVES: The infant mortality rate is considered an important general indicator both of health conditions as the living conditions and development of a population. By presenting certain sensitivity to various external factors, this rate is directly related to economic and social characteristics. It's understood that high infant mortality rates are associated with the needs of socioeconomic conditions. Thus, the factors influencing poverty levels (one-dimensional and multidimensional) on Infant Mortality Rate in Brazil are investigated in this paper. **METHODS:** So it was considered, in addition to analyzing the impact of one-dimensional poverty, which measures poverty only by per capita income, the impact of multidimensional poverty, whose definition incorporates other dimensions, such as sanitation, housing, information, among others. In order to delineate the models, variables such as per capita income, the Gini index and education level were employed for the Brazilian states from 2001 to 2011. Four models were developed to analyze both individually and together impacts of the explanatory variables on the infant mortality rate. For this purpose, panel data was used on fixed and random effects. **RESULTS:** The results showed that decrease the concentration of income and increased educational level, in that order, were the variables which most contributed to the reduction of infant mortality over the period considered. In all, the one-dimensional and multidimensional poverty rates contributed significantly to the reduction of infant mortality rate. However, the ratio of multidimensional poor impact showed a three times higher than the proportion of one-dimensional poor. **CONCLUSIONS:** The findings indicate that it is essential to the formulation of public policies to reduce income concentration allied to improvements in educational conditions, and reduction of multidimensional poverty rates in order to tackle the problems of poor health, and thus reduce the rate of infant mortality.

PRM111

THE ROLE OF PATIENT LEVEL DATA IN ASSESSING HEALTH ECONOMIC VALUE: A CASE STUDY USING EDGE AND THE CORE DIABETES MODEL

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OBJECTIVES: The observational, non-interventional EDGE study showed that a DPP-4 inhibitor, vildagliptin, is efficacious in patients with type 2 diabetes mellitus who have suboptimal glycaemic control on metformin monotherapy in the real-life setting, confirming the results of previous randomised clinical trials. We sought to perform a health economic evaluation using using patient level data (PLD) from EDGE using an established diabetes outcomes model. **METHODS:** The IMS Core Diabetes Model (CDM) was used to evaluate the lifetime costs and quality adjusted life expectancy (QALE) of two different regimens: metformin+vildagliptin compared to metformin+sulphonylurea (SU). Annual therapy costs were: £106.79 (year 1), then £110.51 (year 2+) for metformin+SU and £410.53 (year 1), then £412 (year 2+) for metformin+vildagliptin. Therapy escalation at HbA1c of 8.5% was modelled assuming insulin glargine+metformin (cost £899.51 year 1; £806.84 year 2+). Published meta-analysis data were used for hypoglycaemia rates. Multivariate regression analysis of PLD output from CDM was undertaken using R version 2.15.2. UK costs (£GBP) and health benefits were discounted at 3.5%. **RESULTS:** Mean discounted QALE was 11.01 years (SD 2.5). QALE decreased with increasing age (-0.19 per year, p<0.001) and (-0.18 per year, p<0.001) for metformin+SU and metformin+vildagliptin regimens, respectively. Increasing diabetes duration was associated with a greater decrease in QALE with metformin+SU (-0.18 per year, p<0.001) compared to metformin+vildagliptin (-0.08 per year, p<0.001). Each unit increase in baseline BMI was associated with a -0.12 decrease in QALE for metformin+SU (p<0.001), with no significant difference observed in the metformin+vildagliptin regimen. After adjustment metformin+vildagliptin was associated with a £595.30 reduction in overall costs compared to metformin+SU. **CONCLUSIONS:** The statistical analysis of PLD output provides a mechanism for identifying greatest potential health gains. Despite being positive in all patients, gains in QALE were greater in patients with longer diabetes duration and metformin+vildagliptin regimen compared with metformin+SU under a real-life setting.

PRM112

SURGERY AS AN OUTCOME IN COST-EFFECTIVENESS ANALYSIS

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OBJECTIVES: Surgery in cost-effectiveness analysis can lead to counter-intuitive results, with patients whose disease progresses faster undergoing surgery sooner. As surgery typically results in improved quality of life (QoL) following intervention surgery can have a beneficial impact on ICERs for less successful treatment, in spite of a patient preference to avoid surgery. This study undertook a targeted review of previous NICE technology appraisals in order to assess the impact that surgery has had on decision making in the UK. **METHODS:** A sample of NICE technology appraisals were reviewed to identify papers that have included surgery in their modelled clinical pathways. Key model inputs, results and the impact of surgery on model results were extracted for each study. **RESULTS:** Two technology appraisals were identified that incorporated surgery as a clinical outcome. In TA297, surgery had minimal influence on model results. With both low incidence and no substantial impact of surgery on QoL. In TA329, utility values associated with surgery were 0.7 compared with pre-surgery values ranging from 0.41 to 0.87. Immediate colectomy was found to dominate all non-surgical strategies. If immediate colectomy was excluded as a treatment option, no novel treatments would be cost-effective against conventional care in spite of this being the least effective treatment. Whilst a number of factors contribute to the overall result, the impact of surgery should be quantified. **CONCLUSIONS:** Surgery can have a counter intuitive influence on model results, with a negative event having a long-term positive impact on patient QoL. From this review a number of factors have been found to influence the magnitude of this impact. These include health state utilities before and after surgery, and timing of surgery. Decision rules are required that ensure that surgery is properly accounted for when making decisions, factoring in higher surgical rates into decision making may partly address this issue.

PRM113

TIMED AUTOMATA MODELING OF THE PERSONALIZED TREATMENT DECISIONS IN METASTATIC CASTRATION RESISTANT PROSTATE CANCER

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OBJECTIVES: The Timed Automata modeling paradigm has emerged from Computer Science as a mature tool for the functional analysis and performance evaluation of timed distributed systems. This study is a first exploration of the suitability of Timed Automata for health economic modeling, using a case study on personalized treatment for metastatic Castration Resistant Prostate Cancer (mCRPC). **METHODS:** The treatment process has been modeled by creating several independent timed automata, where an automaton represents a patient, a physician, a test, or a treatment/testing guideline schedule. These automata interact via message passing and are fully parameterized with quantitative information. Messages can be passed, asynchronously, from one automaton to one or more other automata, at any point in time, thereby triggering events and decisions in the treatment process. In the automata time is continuous, and both QALYs and costs can be incorporated using (assignable) local clocks. Uncertainty can be modeled using probabilities and timing intervals that can be uniformly or exponentially distributed. Software for building timed automata is freely available for academic use and includes procedures for statistical model checking (SMC) to validate the (internal) behavior and results of the model. **RESULTS:** In several days a Timed Automata model has been produced that is compositional, easy to understand and easy to update. The behavior and results of the model have been assessed using the SMC tool. Actual results for the mCRPC case study obtained from the Timed Automata model are compared with results of a Discrete Event Simulation model in a separate study. **CONCLUSIONS:** The Timed Automata paradigm can be successfully applied to evaluate the potential benefits of a personalized treatment process of mCRPC. The compositional nature of the resulting model provides a

good separation of all relevant components. This leads to models that are easy to formulate, validate, understand, maintain and update.

PRM114

COST-EFFECTIVNESS ANALYSIS OF SHIZOPHRENIA TREATMENT WITH HALOPERIDOL , OLANZAPINE AND RISPERIDONE IN BOSNIA AND HERCEGOVINA ,REPUBLIC OF SRPSKA BY APPLICATION OF THE MARKOV MODEL

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OBJECTIVES: Schizophrenia is a persistent and costly disease, which requires a continuous antipsychotic treatment. In antipsychotic treatment of schizophrenia, the differences in terms of effectiveness, tolerance, incidence of side effects, relapse and costs have implications regarding the cost-effectiveness. The objective of the specialistic research is to investigate the cost-effectiveness of two second generation antipsychotics (SGA) in treatment of patients with schizophrenia in the RS healthcare system. **METHODS:** The Markov model was developed to assess the medical cost-effectiveness of olanzapine and risperidone (SGA) in relation to haloperidol (FGA) .The cohorts of patients were adult patients diagnosed with schizophrenia . Transitional probabilities were taken over from a major meta-analysis conducted by NICE. The cost considered in this model were taken over from list of rates Health insurance fund (HIF). The utility (in QALY) for remission or relapse were taken over from a scale published by Lenart et al. The cost-effectiveness measure was the Incremental cost-utility ratio (ICUR) . The set threshold was 3200 EUR. **RESULTS:** Undiscounted results of the basic cost-effectiveness analysis show ICUR for olanzapine=912EUR/QALY, ICUR for risperidone = 1528 EUR/QALY. Discounted results show ICUR for olanzapine =877EUR/QALY, ICUR for risperidone=1502 EUR/QALY. Sensitivity analysis has shown , in case of increase in transition probability for relapse by 10%, olanzapine remains a cost-effective strategy, whereas risperidone becomes a cost-ineffective strategy. The sensitivity analysis has also shown the stability of the basic analysis results. **CONCLUSIONS:** No strategy showed itself as dominant, both alternative strategies having higher costs but also higher effectiveness. The model showed that, it takes less money for a better quality in olanzapine than risperidone strategy, while in relation to the set threshold both strategies were cost-effective. Both olanzapine and risperidone have proven cost-effective strategies from the HIF perspective with the recommendation that olanzapine should also be included in the reimbursement list .

PRM116

REVIEWING THE COST-EFFECTIVENESS OF CHEMOTHERAPY AND TARGETED THERAPY FOR METASTATIC BREAST CANCER

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OBJECTIVES: To systematically review and assess the quality of model-based economic evaluations concerning chemotherapy and targeted therapy for metastatic breast cancer (MBC). To analyse the impact of different modelling characteristics on the outcomes of these studies. **METHODS:** The search was performed in PubMED and NHS EED. Inclusion criteria were: English or Dutch language, model-based economic evaluation, chemotherapy or targeted therapy as intervention, population diagnosed with MBC, published between 2000 and October 2014, reporting life-years (LY) or quality-adjusted life year (QALY), and reporting an incremental cost-effectiveness ratio (ICER). Quality of the studies was assessed through a checklist. A standardised extraction sheet was used to retrieve general characteristics, modelling characteristics and results of the studies. **RESULTS:** Twenty-six studies were included and provided fifty-two comparisons. Eighteen studies used a health state-transition model including the following health states: stable/progression-free disease, progression and death. Subgroup analyses were conducted in three studies. Studies were of poor quality. Administration frequency of the regimens, type of model, perspective of the analysis, elicitation method for utilities, total amount of QALY gained and funding source were not always reported. Incremental LY and incremental QALY (iQALY) varied from 0.06 to 1.52 and from 0.05 to 0.60, respectively. Mean incremental cost was €18,977 (range: €-10,690 - €84,174). Mean ICER per LY and per QALY gained were €12,000 (range: €200 - €64,000) and €76,000 (range: €300 - €625,000), respectively. Seven comparisons were represented in two or three studies and were used to analyse the effect of modelling characteristics on the iQALY estimates. **CONCLUSIONS:** The results of the studies were highly variable and the quality of the studies was poor. Comparison of studies was hampered because of under-reporting and the limited number of studies comparing the same regimens. Consequently, no firm conclusions could be drawn concerning the effect of modelling characteristics on outcomes.

PRM117

DECISION-ANALYTIC MODELING STUDIES: AN OVERVIEW FOR CLINICIANS USING DLBCL AS AN EXAMPLE

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OBJECTIVES: Diffuse large B-cell lymphoma (DLBCL) is the most common form of NHL, accounting for up to 30 percent of newly diagnosed cases in the United States and Europe. The purpose of this study was to provide a clinician-friendly landscape of decision-analytic models evaluating different treatment strategies for DLBCL. **METHODS:** A comprehensive search strategy was developed and a systematic literature search in Pubmed and EMBASE from 1996 to June 1, 2015 was queried to identify studies evaluating DLBCL treatment strategies using various decision-analytic models. Studies were screened using pre-defined inclusion criteria after which data from included trials were extracted, by two independent reviewers and disagreements resolved by a third reviewer. We included studies that were published as full-text articles in English, and assessed relevant clinical endpoints, and summarized methodological characteristics (e.g., modeling approaches, simulation techniques, health outcomes, perspectives). **RESULTS:** Seven decision-analytic modeling studies met our inclusion criteria out of the total 289 citations. Major modeling approaches adopted were: decision-tree modeling, Markov state-transition modeling, event based microsimulation/patient level simulation. Health outcomes included survival, number-needed-to-treat, life expectancy, and quality-adjusted life years, time horizon and cycle length. All the studies were critically appraised using quality of health economic scale (QHES) and were found to be of moderate to high quality. Evaluated therapeutic strategies comprised chemotherapeutic combination therapies, stem cell transplantation and supportive care. **CONCLUSIONS:** Our review provides a comprehensive overview of modeling studies assessing treatment of DLBCL which could be used by researchers to develop novel models in DLBCL.

PRM118

ZRX MCDM: A FULLY FLEXIBLE TOOL TO SUPPORT THE LOCAL ADAPTATION OF MULTIPLE-CRITERIA DECISION CRITERIA IN HEALTH CARE

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OBJECTIVES: Multiple-criteria decision analysis (MCDA) is a sub-discipline of operations research that explicitly considers multiple criteria in decision-making environments. Formally structuring complex problems appropriately and considering multiple criteria explicitly leads to more informed and transparent decisions. MCDA methods are increasing in popularity, however existing instruments and approaches are rigid and do not reflect local decision making needs and preferences. ZRx MCDM was developed as a highly flexible tool to support the application of local multiple-criteria decision analysis in health care. This tool was used to evaluate, as an example, three alternatives for the management of anemia associated with chronic kidney disease: Procrit, Aranesp and a Biosimliar (Epogen Zeta). **METHODS:** There are multiple MCDA standard methods that can be applied and the ZRx MCDM tool has been validated against the publications of such methods. Users enter desirable data by selecting an appropriate number of alternatives and criteria relevant to particular decision-making context. Further, criteria scale and weights are defined to obtain results (alternatives in sequence of importance) per different MCDA calculation methods. Seven local decision-makers applied inter-criteria weights using visual analogue scale (VAS). **RESULTS:** Applying the Simple Linear Adaptive Model (SLAM) method, the decision-making criteria as ranked in order of importance were safety, budget impact, cost-effectiveness and unmet medical need (equal third), patient preferences and strategic considerations. Global scores calculated for Aranesp were marginally higher than for the biosimilar (0.52 vs 0.51), whereas Procrit (0.46) scored lower. When Multi Attribute Value Theory (MAVT) method was further applied, total score differentiation was more pronounced: Aranesp, Biosimilar and Procrit (0.57, 0.50 and 0.46). **CONCLUSIONS:** ZRx MCDM tool has been successfully applied in a local decision making context. By not relying on, or promoting, pre-defined criteria, level definitions and weighting/aggregation methods, the tool is fully flexible and adaptive to high precision local decision making needs and preferences.

PRM119

PATENT EXPIRY AND GENERIC PRICING: THE IMPACT ON COST- EFFECTIVENESS RESULTS

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OBJECTIVES: Several studies have considered the change in the price of medicines once a medicines patent expires and exclusivity in the market place is lost. Some HTA bodies consider the implications of patent expiry (e.g. PHARMAC) however the potential impact is not considered in the NICE reference case. The aim of this study was to consider how including the costs of medicines after patent expiry could impact cost-effectiveness results. **METHODS:** A targeted review was conducted to identify any studies which had considered the impact of patent expiry. The approaches were compared and contrasted. A review of recent treatments that have received negative reimbursement decisions from HTA bodies were considered to determine if generic pricing could have influenced the decision making process. **RESULTS:** Patent expiry has potential to impact results, however only in a handful of selected disease areas. The assumptions required to implement generic pricing after patent expiry can be associated with considerable uncertainty, particularly around the generic price of medicine. Further to this, the impact that generic pricing has is dependent on both duration of treatment and life expectancy of modelled populations. **CONCLUSIONS:** Patent expiry offers manufactures a chance to reduce the cost associated with treatment without altering health outcomes. However this is likely to offer a comparable discount to a majority of comparators available in the market, therefore it is likely this will offer the biggest benefit to the manufactures that implement it first.

PRM120

MODEL-BASED TECHNIQUES IN THE EARLY PHASES OF THE MEDICAL DEVICE DEVELOPMENT: A SYSTEMATIC LITERATURE REVIEW

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OBJECTIVES: To systematically review the existing applications of the early model-based techniques to innovative biomedical devices under development. Furthermore, our purpose is to identify their usefulness, limitations, potential improvements, impact on primary stakeholders and implications. Even though the early Health Technology Assessment (HTA) of new medical devices is recognized as an integral part of the technology production, many methodological criticalities still afflict this field. The high level of uncertainty, connected with the scarcity and heterogeneity of data, needs to be faced readjusting the mainstream HTA methodology to support both medical technology producers and policy makers alongside with the R&D process. **METHODS:** Published studies in the English language, related to period 2000-2015, were searched using computerized databases (Pubmed, Scopus, ScienceDirect, Web of Science, IEE Xplore) and reference search of the included articles. All papers that applied the health economic modeling to R&D medical devices met our inclusion criteria. Given the immaturity of the field, we also examined conference proceedings that met the same criteria. **RESULTS:**